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## **Is partial-ALPPS safer than ALPPS? A single-center experience**

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## Is Partial-ALPPS Safer Than ALPPS?

*A Single-center Experience*

Henrik Petrowsky, MD, FACS,\* Georg Györi, MD,\* Michelle de Oliveira, MD, FACS,\* Mickaël Lesurtel, MD, PhD,\* and Pierre-Alain Clavien, MD, PhD, FACS†

The recent introduction of associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) into the clinical practice of hepatobiliary surgery has offered a novel and promising treatment strategy for patients with a variety of primarily nonresectable hepatic tumors.<sup>1,2</sup> Despite the great potential of ALPPS in triggering rapid hypertrophy of parts of the liver, the main concern is the safety of the procedure. For example, the reported mortality in the initial series from Germany was 12%<sup>2</sup> and 15% in a subsequent multicentric analysis,<sup>3</sup> reaching even 27% in experienced hepatobiliary centers.<sup>4</sup> Such figures have triggered the search for better selection criteria and/or technical modification enabling safer surgery.

A recently published analysis of the international ALPPS registry including 202 patients revealed an in-hospital mortality rate of 9% and a severe complication (grade  $\geq 3b$ )<sup>5</sup> rate of 28%.<sup>6</sup> The risk analysis of this cohort suggested that older patients (>60 years of age) and those with noncolorectal liver tumors had poorer prognosis.<sup>6</sup> To better understand the underlying mechanisms and associated harms, we have developed an experimental model of ALPPS that showed that accelerated regeneration in ALPPS is not solely related to parenchymal transection and discontinuation of blood supply between the 2 parts of the liver but mostly due to an “inflammatory-like reaction” leading to enhanced hepatocyte growth.<sup>7</sup> This finding was substantiated by a similar effect on liver regeneration for portal vein ligation associated with kidney, lung, or spleen injuries instead of hepatic transection. Also, we observed in the experimental model that partial (75%–80%) transection of the liver triggered a comparable degree of regeneration of the future liver remnant (FLR) when compared with complete transection. Aside with these novel experimental findings, we have generated the hypothesis, from our early clinical experience, that complete transection of the parenchyma may enhance postoperative liver injury, for example, by causing congestion of the “deportalized” part of the liver. On the basis of our experimental and clinical observations, we developed a new strategy, introduced in 2013 at our institution, to switch from complete transection to a well-defined partial transection (>50% of the transection surface). The rationale behind this idea was our hypothesis that partial ALPPS is safer and achieves similar rapid hypertrophy.

This report presents our experience with partial transection, labeled as partial-ALPPS (both abbreviated as p-ALPPS), compared with ALPPS looking at hypertrophy of the FLR and postoperative outcome. We performed 24 ALPPS procedures in noncirrhotic and noncholestatic patients without major extrahepatic surgery at stage 1

or stage 2 during the period October 2012 to June 2014. Indications for the procedures were colorectal liver metastases ( $n = 16$ ), neuroendocrine tumors ( $n = 2$ ), intrahepatic cholangiocarcinoma ( $n = 2$ ), hepatocellular carcinoma ( $n = 1$ ), hemangiopericytoma ( $n = 1$ ), and other secondary liver tumors ( $n = 2$ ). Eighteen of the 24 procedures were classical ALPPS performed until early 2013 when we switched to p-ALPPS ( $n = 6$ ). Both ALPPS and p-ALPPS were performed by the same surgeons at our institution and solely differed in the degree of liver partition. Although liver transection was complete in all ALPPS procedures (identical to our living related liver transplantation procedures), it involved 50% to 80% of the complete transection plane in the p-ALPPS cohort and was always performed as an anterior approach. Portal vein ligation was performed routinely in each case at stage 1, and intraoperative management and surgical transection techniques were standardized in both groups. Our goal was to transect at least 50% of the future transection plane at stage 1, but the degree of partial transection was determined by anatomic outflow structures (hepatic veins), which we tried to preserve at stage 1 and/or by tumor(s) located within or near the future transection line, which explained the different degree of partial transection ranging from 50% to 80% in this series. Whereas 4 of the 6 patients with p-ALPPS had simultaneous tumor-cleaning procedures of the FLR by wedge resections and/or local ablation techniques using microwave and/or irreversible electroporation (Nanoknife) at stage 1 surgery, 2 patients with p-ALPPS had not.

The p-ALPPS procedures included 3 right hemihepatectomies (segments 5–8), 2 extended right hemihepatectomies (segments 4–8), and 1 left trisectorectomy (segments 1–5 and 8) (Fig. 1).

The sex distribution was similar with a female-to-male percentage of 50%:50% in p-ALPPS and 44%:56% in ALPPS. The median age of the p-ALPPS and ALPPS group was 59 years (range, 25–69 years) and 59 years (range, 33–76 years), respectively. The median standardized FLR before stage 1 was comparable for both groups (p-ALPPS 0.25 vs ALPPS 0.23). We observed a rapid hypertrophy in p-ALPPS, with a median hypertrophy of 60% compared with 61% hypertrophy in ALPPS within a median time of 7 days. Accordingly, the kinetic growth after stage 1 procedure was 15% standardized FLR increase per week for both groups. Even in the light of the fact that other studies reported higher percent hypertrophy in ALPPS in larger cohorts (79%–80%),<sup>2,6</sup> the observed hypertrophy in p-ALPPS seems remarkable and enabled a fast transition from stage 1 to stage 2 operation in our p-ALPPS series. The median time between stage 1 and stage 2 was 11 days (range, 7–21 days) in p-ALPPS and 9 days (range, 7–69 days) in ALPPS. Despite the small sample size of our case series, the data indicate that p-ALPPS triggers rapid hypertrophy, similar to ALPPS, allowing a fast completion of the 2-stage hepatectomy.

We recorded zero in-hospital mortality in p-ALPPS, although 22% of the patients (4/18) died after the conventional ALPPS procedure. The 4 fatalities in the ALPPS group were cardiac failure in 1 patient and liver failure with subsequent multiorgan decompensation in 3 patients. Although no severe postoperative complications (grade  $\geq 3b$ ) were observed after stage 1 procedure in p-ALPPS,

From the \*Department of Surgery, Swiss HPB & Transplantation Center, University Hospital Zurich, Zurich, Switzerland; and †Hospital Paul Brousse, Université Paris Sud, Paris, France.

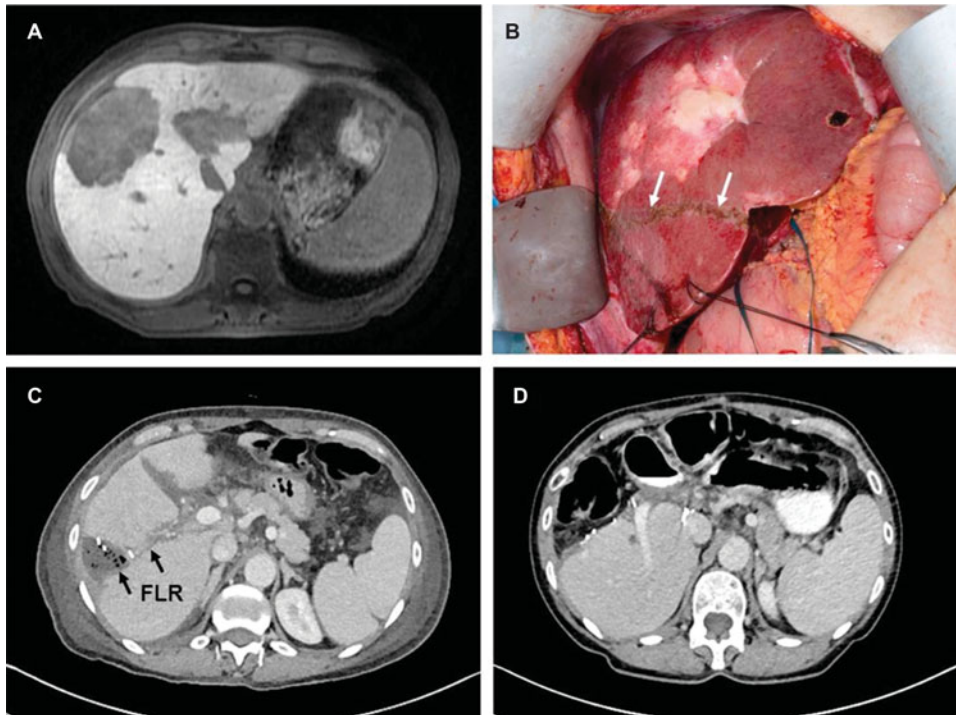
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Reprints: Pierre-Alain Clavien, MD, PhD, FACS, Department of Surgery and Transplantation, Swiss HPB & Transplantation Center, University Hospital Zurich, Raemistrasse 100, CH-8091 Zurich, Switzerland. E-mail: clavien@access.uzh.ch.

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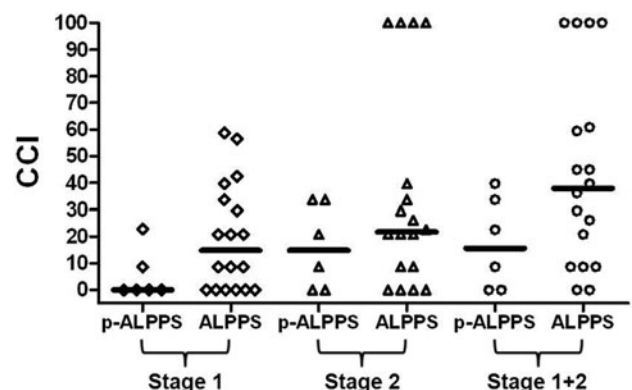


**FIGURE 1.** A 61-year-old female patient with extensive bilobar colorectal liver metastases undergoing curative p-ALPPS procedure. A, Magnetic resonance image shows extensive tumor before stage 1 operation. Only segments 6 and 7 are tumor free. B, The patient underwent partial liver partition between the anterior and posterior right liver sectors with concomitant left portal vein ligation and selective ligation of portal vein branches of the right anterior sector (segments 5 and 8). The line of partial partition was marked with electrocautery after demarcation following selective clamping (arrows). C, Computed tomographic scan on postoperative day 6 after stage 1 operation showing the partial partition line (arrows) and rapid hypertrophy of the FLR (segments 6 and 7). Stage 2 surgery was completed 3 weeks later as left trisectorectomy involving segments 1 to 5 and 8. D, Computed tomographic scan 3 months after stage 2 procedure shows a well-recovered liver remnant after p-ALPPS.

6 of 18 patients (33%) experienced severe complications in the ALPPS group after stage 1 procedure. After stage 2 operation, 6 patients (33%) developed severe complications in the ALPPS group and 2 patients (33%) in the p-ALPPS group. The 2 patients in the p-ALPPS group, however, developed wound-healing problems requiring only surgical revision. The median comprehensive complication index<sup>8,9</sup> was higher in ALPPS for stage 1 (15 vs 0) and stage 2 (22 vs 15) and for both stages (38 vs 15) than that in p-ALPPS (Fig. 2). These data indicate that p-ALPPS is associated not only with zero mortality but also with a trend toward a more favorable postoperative complication profile especially after stage 1 operation. The median length of total intensive care unit stay after stage 1 and stage 2 surgical procedures was 3.5 days for ALPPS and 2 days for p-ALPPS, respectively.

In view of the ongoing and somewhat “passionate” debate about this new challenging procedure, we felt that it is critical to report on safer approaches achieving the same goals. This single-center data suggest that p-ALPPS represents an attractive technical simplification, which, to the best of our knowledge, has not been reported before. The impact of this modification has been encouraging in our center leading to zero postoperative mortality and lower morbidity. Whether such strategy may also be effective in a more extended use of ALPPS, such as in cirrhotic patients or in the presence of perihilar cholangiocarcinoma or gallbladder cancer, remains to be established.

The current data should, of course, be considered with caution due to the nonrandomized, nonmatched study design and the relatively



**FIGURE 2.** In-hospital postoperative morbidity assessed by the CCI. The CCI of each patient undergoing p-ALPPS (n = 6) or ALPPS (n = 18) is presented as scatter plot with medians for stage 1, stage 2, and stage 1 + 2 operations. CCI indicates comprehensive complication index.

small number of patients. This single-center data must, however, be reported and submitted to the experience of others. We speculate that the partial liver partition approach is a safer operation than ALPPS. Partial ALPPS induces a rapid hypertrophy, which, even if perhaps

lower than ALPPS, is sufficient to enable the fast and beneficial second-stage operation leading to complete resection. Because of the very recent practice of ALPPS, and even more so, for p-ALPPS, statements on the oncological outcome cannot be drawn yet. To validate the present findings and to overcome the relatively small sample size, an analysis of collected p-ALPPS cases in the registry should be undertaken as the next step.

Finally, a shortcoming in this new area of liver surgery is the lack of clear terminology. With the aim to facilitate the communication among clinicians regarding the complete (conventional) ALPPS versus p-ALPPS, we propose to standardize the name of p-ALPPS as “partial-ALPPS.”

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